

RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1, 2, 8, 14 and 15 have been amended and no claims have been canceled. Therefore, claims 1 – 6, 8, 14 – 16 and 18 – 65 are currently pending in the application.

B. Rejection of Claims Under 35 U.S.C. §112, First Paragraph

The Action has rejected all pending claims under 35 U.S.C. §112, first paragraph, alleging that the specification does enable a method for inhibiting the growth of a tumor in an individual with the compounds of claim 1.

In response, the Applicants respectfully draw the Examiner's attention, once again, to the arguments set-forth in the Response to Office action date September 24, 2004, incorporated herein by reference in its entirety. Applicants note, that following this response the Examiner stated that "rejections of claims 1-6 and 8 under U.S.C., 112, first paragraph have been overcome..." Applicants content that the Arguments in the September 24, 2004 response address in full the current enablement rejections.

Furthermore, Applicants submit herewith a declaration from Dr. Sanders and Dr. Kline, two of the inventor of the subject application. This declaration and the attached Exhibits are provided as evidence that the current application is enabling of the methods of the current claims. As indicated in the declaration, the efficacy of compounds comprising each of the claimed classes of R groups has been tested. Furthermore, the declaration highlights in particular the effectiveness of compounds comprising an ethylenic R⁵ group, as described in claim 1. Applicants assert that the declaration and the included exhibits demonstrate that instant

specification does enable one of skill in the art to practice the methods of the invention across the full scope of the instant claims.

In particular, the Examiner indicates that undue experimentation would be required to practice the current invention however Applicants respectfully traverse this argument. For example, the Examiner argues that there is little predictability as to whether compounds wherein Y is oxygen or NR⁶ would retain the ability to inhibit tumor growth (page 4 of the current Action). However, studies presented in the specification in Tables 2 and 3 on pages 95 – 98 demonstrates that such compounds do retain antiproliferative properties. For example, compound #1 wherein Y is oxygen demonstrates antiproliferative efficacy against a variety of tumor cell lines (Table 2-1, page 95). On the other hand, compounds #39 and #41 are examples wherein Y is NR⁶ (N-H or N-CH₃, respectively). These compounds also show antiproliferative activity against cancer cell lines as shown in Table 3-2 on page 98. Furthermore, as detailed in the Declaration of Drs. Sanders and Kline the substitution of an ethylenic side chain onto the chroman ring compounds of the instant invention is shown to enhance the antiproliferative effectiveness of the compounds (for example see Table 4 on page 100). In view of these arguments, Applicants assert that undue experimentation is not required to practice the invention across the full scope of the compounds in claim 1.

In yet further arguments the Examiner goes on to cite a portion of *Genentech Inc. V Novo Nordisk A/S* (CA FC) 42 USPQ 2d 1001. However, applicants find it difficult to see the relevance of this citation since the essential finding of the decision was that “when there is **no disclosure of any specific starting material or of any of the conditions under which a process can be carried out**, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the

process is within the skill in the art,” (Genentech Inc. V Novo Nordisk A/S (CA FC) 42 USPQ 2d 1001 (Emphasis added)). Thus, the two flaws identified in the Genentech Inc. V Novo Nordisk decision are clearly not relevant here. First, as stated above, the specification clearly discloses the starting material, that is the compounds of claim 1 and methods for their production in examples 1–3 of the specification. Secondly, the specification clearly provides enabling description for methods of administering the compounds to an individual (*i.e.* the conditions under which the process can be carried out), see the extensive descriptions on pages 12 – 21. In these descriptions the specification teaches preferred dosage ranges, routes of administration and pharmaceutical compositions that may be used according to the invention. Finally, in examples 17–20 *in vivo* methods for using the compounds according to the instant invention are detailed and the *in vivo* efficacy of the chroman ring compounds are further highlighted in the Declaration and Exhibits included therein. Thus, applicants contend that the decision in Genentech Inc. v Novo Nordisk in no way provides a evidence that the present claims are not enabled. In fact, this decision rather indicates that the present claims are fully enabled as described in the forgoing comparisons.

Further in support of these arguments applicants cite *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1440-43 (Fed. Cir. 1995) wherein a pharmaceutical composition was rejected under 35 U.S.C. §112. The composition in *Brana* was rejected because 1) of a failure to describe any specific disease against which the claimed compounds were active, and 2) the tests in the prior art and the Specification were not sufficient to establish a reasonable expectation that the claimed compounds had a practical utility (*i.e.*, antitumor activity in humans). In regards to the second rejection the Commissioner argued that:

Such *in vivo* tests in animals are only preclinical tests to determine whether a compound is suitable for processing in the second stage of testing, by which he apparently means *in vivo* testing in humans, **and therefore are not reasonably predictive of the success of the claimed compounds for treating cancer in humans.**”

In re Brana, 51 F.3d at 1566, 34 USPQ2d at 1442 (Emphasis added).

The Federal Circuit rebuked the Office for requiring this higher standard for proof of therapeutic utility, stating:

The Commissioner, as did the Board, **confuses the requirements under the law for obtaining a patent with the requirements under the law for obtaining government approval to market a particular drug for human consumption.** See *Scott v. Finney*, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994) “Testing for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA). **Title 35 does not demand that such human testing occur within the confines of the Patent and Trademark Office (PTO) proceedings.**”

In re Brana, 51 F.3d at 1566, 34 USPQ2d at 1442 (Emphasis added).

Thus, the decision clearly states that specific pharmacokinetic information is not required to enable a pharmaceutical invention. Thus, the present invention exceeds these requirements with regard to a method for treating an individual. Not only does the specification teach a class of chroman ring compounds that is effectively induce growth arrest and apoptosis in cancer cells it additionally teaches the relative concentrations of each compound that is required to induce apoptosis (see Tables 1–5). Thus, the instant application meets and exceeds the requirements for enablement with respect to the methods of the current claims.

In view of the foregoing arguments and the evidence submitted in the declarations of Drs. Sanders and Kline, Applicants content that the rejections under 35 U.S.C. §112, first paragraph has been rendered moot. The removal of this rejection, is therefore, respectfully requested.

D. Conclusion

This is submitted to be a complete response to the referenced Office Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned at (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.


Respectfully submitted,

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